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CLONING AND CHARACTERIZATION OF THE HUMAN *XRCC9* GENE, WHICH CORRECTS CHROMOSOMAL INSTABILITY AND MUTAGEN SENSITIVITY IN CHO UV40.

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The Chinese hamster CHO mutant UV40 cell line shows pronounced sensitivity to UV and ionizing radiation, simple alkylating agents, and DNA cross-linking agents. The mutant also has a high level (~ 25%) of spontaneous chromosomal aberrations, both breaks and exchanges, and 3-fold elevated sister chromatid exchange level (1). Using functional complementation, we cloned a human cDNA, designated *XRCC9*, that partially corrected the hypersensitivity of UV40 cells to mitomycin C, UV radiation, ethyl methanesulfonate, and cisplatin. The chromosomal aberrations in *XRCC9* cDNA transformants were fully corrected, while the baseline sister chromatid exchange was unchanged. The *XRCC9* genomic sequence was cloned and mapped to chromosome 9p13 by fluorescence *in situ* hybridization. The translated XRCC9 amino acid sequence of 622 amino acids is novel, showing no similarity with known genes. The putative XRCC9 protein is leucine-rich, with several potential dimerization motifs. *XRCC9* shows tissue-dependent expression in both human and baboon tissues. The mRNA expression levels were highest in testis, i.e. ~10-fold and 100-fold greater than in other tissues from human and baboon, respectively. *XRCC9* is a candidate gene for a postreplication repair pathway in mammalian cells. (Work was done under the auspices of the U.S. DOE by LLNL under contract No. W-7405-ENG-48).

1. Busch et al., A CHO mutant, UV40, that is sensitive to diverse mutagens and represents a new complementation group of mitomycin C sensitivity. Mutat. Res. 363, 209-221, Mutation Research. 363. 209-221, 1996.